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[illegible] LABORATORY OF
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A RESEARCH LABORATORY fortunate enough to be closely associated with an active hospital can profitably take advantage of the numerous opportunities arising from the clinic. Because of the nature of clinical problems, the research program must be sufficiently flexible to be adapted to the problem of the moment. Accordingly, the activities of the Howe Laboratory are characteristically diverse and do not lend themselves to categorical listing. Yet there are always main lines of investigation which, varying somewhat from year to year, have nevertheless a measure of continuity. Falling into this category during the past year have been the studies on intra-ocular fluid dynamics, effects of radiant energy on the eye, and stereophotography of the anterior segment of the eye.

Intra-Ocular Fluid Dynamics

Curiously, and quite fortuitously, Dr. Kinsey and Dr. Grant have directed their respective attentions to opposite ends of the intra-ocular fluid cycle. Dr. Kinsey, continuing his studies primarily on the formation of aqueous humor, has presented a unified concept of the dynamics of the aqueous humor which can account for the relative concentration of the constituents of this fluid compared with that of plasma. It also offers an explanation for the intra-ocular pressure of normal eyes and eyes showing various pathologic conditions. This concept involves the production of unbalanced hydroxyl ions, as suggested by Friedenwald, and the simultaneous diffusion of all the constituents of the plasma into and out of the posterior chamber. The hydroxyl ions, by reaction with carbon dioxide, are converted to bicarbonate ions, which are electrically neutralized by sodium and other cations diffusing from the blood. The salts formed diffuse into the posterior chamber, thereby maintaining the aqueous humor hypertonic to the plasma. As a result of this hypertonicity, more water diffuses into the posterior chamber than diffuses out again; i.e., there is a net transfer of water into the posterior chamber. The excess transfer of water into the posterior chamber dilutes the other substances which are diffusing to and fro between the blood and the posterior chamber so that, at steady state these substances exist in lower concentration in the aqueous humor than in plasma. The aqueous humor thus "formed" flows between the iris and the lens into the anterior chamber, where there is a further exchange of water across the iris. The electrolytes do not exchange, however, because the walls of the blood vessels of the iris are impermeable to ions under normal conditions. All the constituents of the aqueous humor of the anterior chamber then escape by flow from the eye at the angle at a rate of about 3 microliters per minute. The influx of water as a result of hydrostatic and osmotic pressures, particularly the latter, is responsible for the intra-ocular pressure. The magnitude of the pressure depends on the rate of production of hydroxyl ions in the epithelium of the ciliary body, the ease of outflow at the angle and, to a less extent, the porosity of the blood-aqueous barriers. Under normal conditions these factors are in balance with a hydrogen ion concentration of the aqueous exceeding that of the plasma by 0.17 pH unit. Under abnormal conditions they may vary independently and give rise to either an increase or a decrease in intra-ocular pressure.

Dr. Grant has been concerned primarily with discovery of the nature of the alterations in the outflow of aqueous humor which are associated with ocular disease in patients. This study has utilized the "tonographic" method which was developed last year for measuring the facility of escape of aqueous from the human eye and the net rate of flow or formation of aqueous. The method has so far been applied in making some 800 measurements on 400 eyes in patients and normal volunteers. These measurements have provided direct evidence where previously there was mainly conjecture. It appears, for instance, to have been established by this study that an abnormal resistance to the escape of aqueous is the rule in glaucoma rather than any excessive formation or secretion of fluid into the eye. The success of surgical or medical treatment appears at present to depend principally upon improvement of the facility of outflow of the aqueous from the eye. Particularly interesting has been the finding that early in the development of so-called wide-angle primary glaucoma an abnormal resistance to aqueous outflow can be detected even when the intra-ocular pressure is normal. Tonography thus presents a method which is not only proving most useful in the investigation of the mechanisms of glaucoma but also provides a means for early diagnosis of the most common form of this disease. There can be little doubt that this study of Dr. Grant's comprises one of the most important contributions that has been made pertaining to the problem of glaucoma in recent times.

RADIANT ENERGY

Under the auspices of the National Research Council and Atomic Energy Commission two projects have been undertaken in the Howe Laboratory during the past year directed primarily toward the understanding of radiation cataracts. Dr. Cogan and Dr. Donaldson have been concerned with the cataractogenic dose of x-rays and the morphogenesis of radiation cataracts in animals and human beings, while Dr. Kinsey and Dr. Merriam have been concerned with the effect of x-rays and neutrons on the synthesis of glutathione and protein in the lens. Dr. Cogan also spent two months at Los Alamos where, in conjunction with Dr. John Goff, a series of experiments were set up to determine the cataractogenic dose of neutrons having different energies.

STEREOPHOTOGRAPHY

Three-dimensional photographs are so much more informative and aesthetic than the conventional flat photographs that there can be little doubt they will largely replace the current methods of pictorial presentation wherever possible. To this end Dr. Donaldson has developed further his stereocamera and stereoprojector, and an impressive series of clinical photographs are being collected by Drs. Donaldson and Cogan for subsequent use as teaching material, possibly in the form of an Atlas. The method has already been used effectively in teaching neuro-ophthalmic anatomy in the postgraduate course and for clinical demonstrations to small groups. An exhibit of some of the photographs was awarded first prize at the annual meeting of the American Academy of Ophthalmology and Otolaryngology.

MISCELLANEOUS

Of the diverse activities with which the Howe Laboratory has been concerned during the past year mention may be made of the following:

Drs. Kinsey and Merriam have continued their investigations of the synthesizing mechanisms operating in the ocular rabbit lens. Lenses are cultured in vitro for various periods in the presence of glycine labeled with radioactive carbon, and the protein was hydrolyzed to its constituent amino acids. These were then separated chromatographically on a starch column and tested for radioactivity. It was observed that radioactive glycine had become incorporated into the protein and that some of the glycine had been transformed into serine which in turn had become incorporated into the lens protein. From the rate at which these reactions occurred it was concluded that about 2½ to 5 per cent of the protein of the young rabbit lens is turned over each day.

Drs. Kinsey and Merriam made a detailed study of the amino acid composition of aqueous humor by means of starch column chromatography. A similar investigation of the amino acid composition of young rabbit lenses was also made.

Continuing his long-term studies on pharmacology and toxicology of the eye, Dr. Grant has further investigated the ocular effects of quarternary ammonium compounds with particular attention to the unusually potent muscarinic compound which last year was found to be effective in lowering the pressure in glaucoma but unfortunately had unpleasant systemic side effects. This compound has been found like other miotic drugs to facilitate the outflow of aqueous. Some progress has been made in eliminating the systemic side effects, and the compound is still being investigated clinically in treatment of glaucoma.

Studies have been initiated to compare synthetic sympathin E with epinephrine in their action on the eye. This comparison appears of interest, particularly in relation to glaucoma, because the sympathin appears to have considerably less dilating effect on the pupil than does epinephrine, although the vascular effects of the two substances are of comparable intensity. A related drug Isuprel was found not to dilate the human pupil on topical application even of quantities which caused unpleasant cardiovascular effects.

Two newly available drugs, Artane and Parpanit, were investigated for use in the eye as possible atropine substitutes. These substances had considerable effect on the pupil and accommodation, but they were found to be much too irritating to the cornea.

Investigations were carried out by Dr. Grant on the toxicity to the eye of numerous substances, some of which had been specifically suspected of causing disturbances in patients. The substances investigated included chromium and lead compounds, formaldehyde, certain phenolic compounds, relatives of maleic acid, plastics, detergents and hair-waving preparations. Several potential agents for dissolving rust deposits from the cornea were investigated, but so far all have been excessively irritating to the cornea.

Together with Dr. Paul A. Chandler, Dr. Grant designed an iris forceps which is intended to minimize the chances of trauma to the lens.

Dr. Kinsey has continued to supervise the research program of the Massachusetts Eye and Ear Infirmary concerned with retrolental fibroplasia. During the past year emphasis has been placed on studying the effect of the prophylactic use of vitamin E, and more recently weekly transfusions of whole maternal blood, on the course and incidence of retrolental fibroplasia in all premature infants weighing less than four pounds born at the Boston Lying-in Hospital. During this period the incidence of the earlier stages of the disease appears to be uninfluenced by the prophylactic measures taken, but the disease has not progressed as far in the affected eyes as it did in previous years.

Teaching again occupied a prominent place by members of the Laboratory both in organized postgraduate courses and in informal seminars.

The Howe Library, under the able guidance of Miss Jeanette Loessl, has continued its valuable service to the local medical and scientific community. In addition to the ophthalmic collection, which is one of the finest in the country, the Library now houses part of the ear, nose and throat collection.

Changes in Personnel

During the past year the Howe Laboratory lost Dr. Elek J. Ludvigh and Dr. V. Everett Kinsey.

Dr. Ludvigh had been a staff member of the Howe Laboratory since its inception and had done much to develop the Laboratory into what it is today. His fundamental researches in physiologic optics and numerous contributions in other fields of ophthalmic research and teaching occupy an important place in our present day science. Dr. Ludvigh resigned to become Director of Research at the Kresge Eye Institute, where he will carry on research and teaching in physiologic optics. He will be Professor of Ophthalmic Physics at Wayne University Medical School.

Dr. V. Everett Kinsey had been a staff member and one of the Laboratory's chief supports for almost 11 years. Through his researches in biochemistry of the eye he has attained the stature of a leading authority in this field and set a pattern that others might emulate. Dr. Kinsey resigned to become Assistant Director of Research at the Kresge Eye Institute, where he will continue his investigations and teaching. He will be Professor of Ophthalmic Biochemistry at Wayne University Medical School.

There can be no denying that the loss of these two scientists is a severe blow to the Howe Laboratory, but there can also be no denying that the Howe Laboratory is serving a useful purpose by making available seasoned investigators to a new research center. Such a function may become of increasing importance as the number of new ophthalmic research centers throughout the country increases.

Finances

While no substantial addition has been made during the past year to the endowment for fellowships or permanent subsidy, various friends of the Laboratory have made substantial contributions to offset the current expenses and to make possible a small measure of expansion. These contributions are entirely unsolicited and go a long way, both spiritually and practically, toward making the Laboratory operations successful.

In the past few years there have arisen many money-raising campaigns for eye research throughout the country, and the Howe Laboratory finds itself in active competition for philanthropic support. Knowing full well how the public is surfeited with appeals for money, the Laboratory does not propose to add further to this burden. Instead it will continue to depend for growth and development on the spontaneous giving of those who see in it the worthy investment that we believe it to be.

A specific note of gratitude is in order to the following who have generously contributed during the past year to the Howe Laboratory:

For general expenses:
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DAVID G. COGAN, M.D.
Director

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